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Letter to the Editor: "Arteriovenous Fistula: A Complication Following Renal Biopsy of Suspected Bilateral Wilms Tumor"

There is an alternative approach to the treatment of a patient with a stage IV nephroblastoma reported by Coppes et al. [1] in the June issue of this journal. The question in that particular patient was whether or not an ultrasonographic (and CAT scan-confirmed) finding in the contralateral right kidney was neoplastic. One might form an opinion on the malignant nature of such a mass, depending on whether it did or did not respond to chemotherapy.

The SIOP strategy in the described patient would have been pretreatment for stage IV disease with a three-drug regimen, and evaluation of the abdominal and pulmonary sites before surgery. One would have thus been informed about the response of the tumour in the left kidney, the response of the abnormality in the right kidney, and the response of the pulmonary lesions. Even at this time there still would have been the option of a biopsy on the right side. Had there been no change in the lesion on the right with the localization and the difference in echotexture as mentioned in the paper and shown in Figure 2, there could have been reason for observation rather than biopsy, thereby avoiding the risk of the reported complication.

This lesion was well defined and readily available for follow-up. Even small changes could have been detected early and treated appropriately.

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Reply

First, I thank Dr. de Kraker for his valuable and stimulating comments. His remarks reflect the fundamental difference between the therapeutic approach favored by the International Society of Paediatric Oncology (SIOP) and the one advocated by the National Wilms Tumor Study Group (NWTSG). SIOP investigators recommend therapy based on findings obtained at surgery preceded by chemotherapy, the NWTSG grounds treatment on the clinicopathologic findings at diagnosis. The advantages and disadvantages of both approaches have been discussed elsewhere [1,2].

Dr. de Kraker's proposal is reasonable; that is, to give preoperative chemotherapy to patients with synchronous bilateral Wilms tumor and to do so without obtaining histopathologic confirmation. Many patients would be managed well following this approach. My own preference, however, is to be more individualized.

Data from the NWTSG demonstrate several important histopathologic points. First, the incidence of anaplasia in synchronous bilateral Wilms tumor is approximately 10% (15 patients among 145 registered on NWTS studies 2 and 3 [3]. Second, six among the 15 (40%) had discordant histology, that is, favorable histology (FH) on one side and anaplasia on the contralateral side. Thus, about 10% of children with synchronous bilateral Wilms tumor will have anaplastic histology, and biopsy of only one side will be misleading in almost half of those patients. Since neither size nor location of a childhood renal tumor correlates with histology, only biopsy of each lesion will yield this information. The search for anaplasia is important in children with bilateral Wilms tumor because it carries the same adverse prognostic significance as in unilateral Wilms tumor [3]. Consequently, finding stage II or higher diffuse anaplasia in either tumor dramatically changes the therapy recommended by the NWTSG: dactinomycin is omitted and cyclophosphamide, etoposide, doxorubicin, and radiation therapy are added [4]. Moreover, even if the tumors on both sides were to feature FH characteristics, it remains important for those following NWTSG guidelines to determine the local stage on each side since FH stage III disease calls for the use of local radiation [4]. Thus, an individualized diagnostic approach in patients with synchronous bilateral Wilms tumor allows one to identify early on what is considered to be the most appropriate therapy and as a consequence provide each patient with the best chance of survival.

In conclusion, Dr. de Kraker's comments are stimulating and form an invitation to remain critical with regard to one's own practice. There remains, however, room for honest disagreement. In our particular patient, determination of the histology and the local stage of each

side was considered important for the reasons given above.

Finally, despite the complication experienced by this patient, we have more often regretted not having performed biopsies in children with cancer who presented with masses of unclear nature, than the other way around. As a result, we have come to advocate the slogan ''when in doubt, get a tissue diagnosis.''

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Letter to the Editor: ''Pancreatoblastoma in Childhood: The Role of Alpha-Fetoprotein''

Pancreatoblastoma is a rare tumor occurring in infancy and childhood. It was first described in 1977 by Horie et al. [1]. Since then 29 children with pancreatoblastoma were reported in the literature [2–18]. Alpha-fetoprotein is a known marker in serum and tumor tissue of patients with pancreatoblastoma. We were interested in the role of elevated serum AFP in this disease.

A 3-year-old caucasian boy presented with pancreatoblastoma having a characteristic large intra-abdominal mass. There was no detectable metastatic disease. Laboratory findings included elevated serum levels for AFP of 3113 ng/ml (normal, 0–15) and lactate dehydrogenase of 542 IU/L (normal, 40–230). The tumor was removed in toto. Within 17 days postoperatively the serum AFP declined to 74 ng/ml and was within the normal range after 4 weeks. Postoperative chemotherapy was started with cisplatin, etoposide, and bleomycin and continued over 3 months. Thirteen months after diagnosis, metastases to the liver were diagnosed. The histological findings again met the criteria of pancreatoblastoma although the AFP serum concentrations stayed within normal limits. At the time of relapse the boy was treated with chemotherapy consisting of ifosfamide and etoposide followed by idarubicin for 7 and 6 months respectively. He remains well 3 years after diagnosis, 10 months after his last chemotherapy.

The presentation and course of pancreatoblastoma in childhood is not predictable. Characteristics of presentation are young age, male predominance, histology with high rate of mitosis and invasive growth, and elevated serum AFP values in some children [8]. Metastases may be present at diagnosis or develop later. It is unclear whether elevated serum AFP or positive AFP staining in tumor tissue is correlated with metastatic disease, recurrence, or residual disease. Table I summarizes the data of our patient and 29 children with pancreatoblastoma reported in the literature. Eight patients reported by Lack [19] are not included because of a different histological description. Newborns with Beckwith-Wiedemann syndrome are also excluded.

Ten of 29 patients had elevated serum AFP values (AFP-positive) at diagnosis, in 19 patients the AFP serum concentration was not mentioned, and in one patient it was within normal range (AFP-negative) [9]. Surgery was the primary therapy in most of the patients, and the sole therapy in 18 of 30 children. Four children were started on chemotherapy up-front [4,5,7,9]. In a few patients chemotherapy or radiotherapy was initiated at the time of relapse. Metastases or local recurrence of the tumor was noted in 12 children with a predominance of the AFP-positive group. Relapses occurred between 8 months and 3.5 years after diagnosis. Two patients of the AFP-positive group had metastases to the liver at the time of diagnosis [8]. Whether serum AFP levels were increased at the time of relapse or with the presence of metastases respectively is not conclusively documented. In two patients with elevated serum AFP at the time of diagnosis AFP was found to be increased at the time of dissemination [4,5]. Thirteen of 29 patients died of disease, 2 children [8,16] during or immediately following surgery. Follow-up is unknown in 3 patients. In most of the children, metastatic disease resulted in death.

The data from the literature do not clarify the significance of elevated AFP concentrations in serum or tumor tissue vis-a-vis the behavior of the tumor. AFP is a useful marker in patients with pancreatoblastoma provided it is

TABLE I. Clinicopathological Findings and AFP

Group	No	Sex m/f	Age (years) Median	Age (years) Range	Size of Tumor + Median	Size of Tumor + Range	Metastases #	Follow-up NED	Follow-up DOD	References
AFP-positive	10	6/4	4.5	1.8–8	12.5	6–8	8/10	5	5	2–8
AFP-negative	1	1/0	3		7		—		1*	9
AFP-level not reported	19	11/8	5	1.3–13	11	4–17	4/19	9	8 2*	1, 8, 10–18 18

NED, no evidence of disease; DOD, died of disease.
+ maximum diameter (cm), *follow-up not reported, # metastasis and local recurrence.

elevated. Similar to AFP-secreting yolk sac tumors it may be a useful marker in the follow-up after surgery and during chemotherapy. However we learned from our patient that it does not necessarily correlate with disease activity, disease recurrence or the presence of metastases.

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